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PATENT

**UNITED STATES PATENT AND TRADEMARK OFFICE**  
(Case No. 96-223-ZZ)

IN THE APPLICATION OF:

Tamburini et al.

Serial No. 09/974,026

Filed: October 10, 2001

Title	Human Bikunin
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Examiner: Not yet assigned

Group Art Unit: Not yet assigned

BOX DD  
Commissioner for Patents  
Washington, D.C. 20231

Sir:

## TRANSMITTAL LETTER

In regard to the above identified application:

1. We are transmitting herewith the attached:
  - a. Information Disclosure Statement;
  - b. Form PTO-1449;
  - c. Copy of IDS Citations (58 references); and
  - d. Return Receipt Postcard.

2. With respect to additional fees:

☒ No additional fee is required.

3. Please charge any additional fees or credit overpayment to Deposit Account No.13-2490. A duplicate copy of this sheet is enclosed.

4. CERTIFICATE OF MAILING UNDER 37 CFR § 1.8: The undersigned hereby certifies that this Transmittal Letter and the paper, as described in paragraph 1 hereinabove, are being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Box DD, Washington, D.C. 20231 on this 12<sup>th</sup> day of March, 2002.

By :

Stephen H. Docter  
Stephen H. Docter  
Reg. No. 44,659



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# PATENT

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE (Attorney Ref. No. 96-223-ZZ)

In re the Application of:	)	
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<b>Tamburini et al.</b>	)	Examiner: <b>not yet assigned</b>
	)	
Application No.: <b>09/974,026</b>	)	Group Art Unit: <b>not yet assigned</b>
	)	
Filing Date: <b>October 10, 2001</b>	)	
	)	
For: <b>Human Bikunin</b>	)	
	)	

### INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents  
Washington, D.C. 20231

Sir:

This statement is filed under 37 C.F.R. §§1.97-1.98, in compliance with the duty of disclosure set forth in 37 C.F.R. §1.56. A PTO Form 1449 is enclosed. In addition, copies of the references listed on the Form 1449 are enclosed. These documents contain information that the Patent Office may consider to be important in deciding whether to allow the present application to issue as a patent.

In accordance with MPEP §§ 609 and 707.05(b), it is requested that the references cited (including any cited in the specification which are not repeated on the enclosed Form 1449) be given thorough consideration and that they be cited of record in the prosecution history of the present application by initialing on the Form 1449. Such initialing is requested even if the Patent Office does not consider a cited reference to be sufficiently pertinent to use in a rejection, or otherwise does not consider it to be prior art for any reason, or even if the Examiner does not

believe that the guidelines for citation have been fully complied with. This is requested so that each document becomes listed on the face of the patent issuing on the present application.

Two of the references enclosed are entirely in a foreign language. English translations of the references are not available to the applicants. However, the English Medline database entries for the two references are as follows:

Reference 49:

Arzneimittelforschung 1975 Jan;25(1):110-6

**[Effect of the protease inhibitor aprotinin on pulmonary function and on the inhibitory activity of sputum in patients with chronic obstructive bronchitis]**

[Article in German]

**Rasche B, Marcic I, Ulmer WT.**

It has been investigated whether a substitution of protease inhibitor deficiency is indicated in case of chronic obstructive airway disease. As a therapeutic possibility, apronitin isolated from bovine organs (tyasylol), which in vitro inhibits sputum proteases up to 80 per cent was tested. Besides infusion, inhalation was chosen for application by which a protease inhibition could be attained. We observed an inhibition of the course of illness associated with a good tolerance of the preparation. Whether a therapy applying the addition of protease inhibitor is reasonable in the long run in chronic diseases cannot yet be concluded from these investigations.

Reference 52:

Med Klin 1977 Feb 4;72(5):145-60

**[Drug therapy of bronchosecretolytic disorders]**

[Article in German]

**Schmidt OP.**

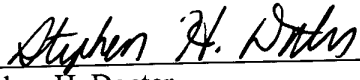
Publication Types:

Review

If there is any fee due in connection with the filing of this Statement, Applicants hereby authorize the Commissioner to charge the fee to Deposit Account No. 13-2490.

Respectfully submitted,  
McDonnell Boehnen Hulbert & Berghoff

Dated: March 12, 2002

By:   
Stephen H. Docter  
Reg. No. 44,659

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Substitute for form 1449A/PTO

# **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Complete if Known

Application No.	09/974,026
Filing Date:	10/10/2001
First Named Inventor	Tamburini
Group Art Unit	Not yet assigned
Examiner Name	Not yet assigned
Attorney Docket No.	96-223-ZZ

Sheet	1	Of	4
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## **U.S. PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines Where Relevant Passages or Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
	1	5,106,833		Bronze, Jr. et al.	04-21-1992	
	2	5,223,482		Schilling, Jr. et al.	07-29-1993	
	3	5,312,736		Rasmussen et al.	05-17-1994	
	4	5,403,484		Ladner et al.	04-04-1995	
	5	5,407,915		Fritz et al.	04-18-1995	
	6	5,436,153		Sprecher et al.	07-25-1995	
	7	5,441,931		Sprecher et al.	08-08-1995	
	8	5,541,288		Nakano et al.	07-30-1996	
	9	5,576,294		Norris et al.	11-19-1996	
	10	5,663,143		Ley et al.	09-02-1997	
	11	5,677,146		Sprecher et al.	10-14-1997	
	12	5,728,674		Sprecher et al.	03-17-1998	
	13	5,731,412		Shimomura	03-24-1998	
	14	5,736,364		Kelley et al.	04-07-1998	
	15	5,747,449		Lasters et al.	05-05-1998	
	16	5,786,328		Dennis et al.	07-28-1998	
	17	5,795,865		Markland et al.	08-18-1998	
	18	5,834,244		Dennis et al.	11-10-1998	
	19	5,854,396		Shimomura et al.	12-29-1998	

Examiner Signature		Date Considered	
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\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>6</sup> Applicant is to place a check mark here if English translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you spent on this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington DC 20231 DO NOT SEND

FOREIGN PATENT DOCUMENTS								
Examiner Initials*	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines Where Relevant Passages or Figures Appear	T <sup>6</sup>
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
	20	EP	0 439 442	B1	Washington Univ.	03-06-96		
	21	EP	0 563 389	A1	Zhyrnov, Oleg Petrovich	10-06-93		
	22	EP	0 758 682	A2	Mitsubishi Chemical Corp.	02-19-97		
	23	WO	92/15605	A2	Protein Engineering Corp.	09-17-92		
	24	WO	93/14120	A1	Novo Nordisk A/S	07-22-93		
	25	WO	95/18830	A2	Protein Engineering Corp.	07-13-95		
	26	WO	96/03503	A1	The Green Cross Corp.	02-26-97		
	27	WO	96/35788	A2	Scios, Inc.	11-14-96		
	28	WO	97/33996	A2	Bayer Corp.	09-18-97		
	29	WO	98/33920	A2	Human Genome Sciences, Inc.	08-06-98		

OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and-or country where published	T <sup>2</sup>
	30	APP, E.M., KING, M., HELFESRIEDER, R., KOHLER, D., AND MATTHYS, H. (1990) Acute and long-term amiloride inhalation in cystic fibrosis lung disease. A rational approach to cystic fibrosis therapy. <i>American Review of Respiratory Disease</i> 141, 605-612.	
	31	CHRAIBI, A., VALLET, V., FIRSOV, D., HESS, S.K., AND HORISBERGER, J.D. Protease modulation of the activity of the epithelial sodium channel expressed in xenopus oocytes. <i>Journal of General Physiology</i> 111(l): 127-13 8, 1998.	
	32	DELARIA, K.A., MULLER, D.K., MARLOR, C.W., BROWN, J.E., DAS, R.C., ROCZNIK, S.O. AND TAMBURINI, P.P. Characterization of placental bikunin, a novel serine protease inhibitor. <i>Journal of Biological Chemistry</i> 272(18):12209-12214, 1997.	
	33	DENDA, K. Genbank accession no. AB006534. "Homo sapiens mRNA for hepatocyte growth factor activator inhibitor type 2, complete cds." 04-Mar-1998.	
	34	DIETRICH, W. et al. (1989) Thorac. Cardiovasc. Surg. 37:92-98.	
	35	HILLIER, L. et al. EMBL/Genbank accession no. N39798. "The WashU-Merck EST Project." January 26, 1996.	
	36	HILLIER, L. et al. EMBL/Genbank accession no. R35464. "The WashU-Merck EST Project." May 4, 1995.	
	37	HILLIER, L. et al. EMBL/Genbank accession no. R74593. "The WashU-Merck EST Project." June 9, 1995.	
	38	KAWAGUCHI, T., QIN, L., SHIMOMURA, T., KONDO, J., MATSUMOTO, K. DENDA, K., AND KITAMURA, N. (1997) "Purification and cloning of hepatocyte growth factor activator inhibitor type 2, a kunitz-type serine protease inhibitor" J. Biol. Chem. 272:27558-27564.	

Examiner Signature	Date Considered
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OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS, CONT.			
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	39	LINDBERG, S., AND OLSSON, H., 1991 "Tissue Kallikrein Stimulates Mucociliary Activity in the Rabbit Maxillary Sinus," <i>Acta Oto-Laryngologica</i> , 111, (6) pp. 1126 - 1132.	
	40	MARLOR, C.W., DELARIA, K.A., DAVIS, G., MULLER, D.K., GREVE, J.M., AND TAMBURINI, P.P. Identification and cloning of human placental bikunin, a novel serine protease inhibitor containing two kunitz domains. <i>Journal of Biological Chemistry</i> 272(18):12202-12208, 1997.	
	41	MATHEWS, L.W., SPECTOR, S., LEMM, J., AND POTTER, J.L. Studies on Pulmonary secretions. I. The Overall Chemical Composition of Pulmonary Secretions from Patients with Cystic Fibrosis, Bronchiectasis, and Laryngectomy. <i>American Review of Respiratory Disease</i> 88:199-204, 1963.	
	42	MCAULAY, A.E., CROSSLEY, J., PLACE, G.A. AND POLL, C.T. Effect of UTP on ion transport in tertiary cultures of human bronchial epithelial (HBE) cells. <i>Pediatric Pulmonology</i> S 17, Abs 141, 1998.	
	43	MIYAZAWA, K. et al. (1996) "Activation of hepatocyte growth factor in the injured tissues is mediated by hepatocyte growth factor activator" <i>J. Biol. Chem.</i> 271:3615-2618.	
	44	NEWTON, B.B. AND HALL, R.L. Mucociliary clearance in the guinea-pig is increased by ouabain (i.v.) and by hypertonic saline (14.4%) aerosol. in <i>Cilia, Mucus and Mucociliary Interactions</i> . Ed. Baum, G.L., Priel, Z., Roth, Y., Liron, N., Ostfeld, E., Marcel Dekker. New York. 1998.	
	45	NEWTON, B.B., POLL, C.T. AND HALL, R.L. Inhalation of amiloride increases tracheal mucus velocity and decreases tracheal potential difference in the guinea-pig. <i>Pediatric Pulmonology</i> S17, Abs 364, 1998.	
	46	O'RIORDAN, T.G., MAO, Y.M., OTERO, R., LOPEZ, J., SABATER, J.R., AND ABRAHAM, W.M. Budesonide affects allergic mucociliary dysfunction. <i>Journal of Applied Physiology</i> 85(3):1086-1091, 1998.	
	47	O'RIORDAN, T.G., OTERO, R., MAO, Y.M., LAUREDO, I., AND ABRAHAM, W.M. Elastase contributes to antigen-induced mucociliary dysfunction in ovine airways. <i>American Journal of Respiratory &amp; Critical Care Medicine</i> 97(5):1522-1528, 1997.	
	48	POTTER, J.L., MATTHEWS, L.W., SPECTOR, S., AND LEMM, J. Studies on pulmonary secretions. II. Osmolality and the ionic environment of pulmonary secretions from patients with cystic fibrosis, bronchiectasis, and laryngectomy. <i>American Review of Respiratory Disease</i> 67(1):83-87, 1967.	
	49	RASCHE, VON B., MARCIC, I., AND ULMER, W.T., 1975 "Über die Wirkung des Proteaseinhibitors Aprotinin auf die Lungenfunktion sowie die inhibitorische Aktivität des Sputums bei Patientin mit chronisch-obstruktiver Bronchitis" <i>Arzneimittel-Forschung (Drug Res.)</i> 25, Nr.(1) 110-116.	
	50	ROBINSON, et al., 1997. "Effect of increasing doses of hypertonic saline on mucociliary clearance in patients with cystic fibrosis," pp. 900.	
	51	ROBINSON, M., HEMMING, A.L., REGNIS, J.A., WONG, A.G., BAILEY, D.L., BAUTOVICH, G.J., KING, M., AND BYE, P.T.P. Effect of increasing doses of hypertonic saline on mucociliary clearance in patients with cystic fibrosis. <i>Thorax</i> 52(10):900-903, 1997.	
	52	SCHMIDT, O.P., 1977, "Medikamentöse Therapie bronchosekretorischer Störungen" <i>Medizinische Klinik</i> . 72 (5), 145-160.	
	53	SHIMOMURA, T. et al. (1997) "Hepatocyte growth factor activator inhibitor, a novel kunitz-type serine protease inhibitor" <i>J. Biol. Chem.</i> 272:6370-6376.	
	54	TOMKIEWICZ, R.P., APP, E.M., ZAYAS, J.G., RAMIREZ, O., CHURCH, N., BOUCHER, R.C., KNOWLES, M.R., AND KING, M. Amiloride inhalation therapy in cystic fibrosis. Influence on ion content, hydration, and rheology of sputum. <i>American Review of Respiratory Disease</i> 148(4 Pt 1):1002-1007, 1993.	
	55	VALLET, V., CHRAIBI, A., GAEGGELER, H.P., HORISBERGER, J.D., AND ROSSIER, B.C. An epithelial serine protease activates the amiloride-sensitive sodium channel. <i>Nature</i> 389(6651):607-610, 1997.	
	56	WILLS, P.J., GARCIA SUAREZ, M.J., RUTMAN, A., WILSON, R., AND COLE, P.J. The ciliary transportability of sputum is slow on the mucus-depleted bovine trachea. <i>American Journal of Respiratory &amp; Critical Care Medicine</i> 151(4):1255-1258, 1995.	
	57	WILLS, P.J., HALL, R.L., CHAN, W.M., AND COLE, P.J. Sodium chloride increases the ciliary transportability of cystic fibrosis and bronchiectasis sputum on the mucus-depleted bovine trachea. <i>Journal of Clinical Investigation</i> 97(11):9-13, 1997.	

Examiner Signature	Date Considered
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**OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS, CONT.**

58	WOJTA et al. (1994) "Hepatocyte growth factor stimulates expression of plasminogen activator inhibitor type 1 and tissue factor in HepG2 cells" Blood 84:151-157 (Abstract).	
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Examiner Signature		Date Considered	
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